DETAILED ACTION

Receipt is acknowledged of amendment filed on January 13, 2010. Claims 1-3, 5-21 are pending.

Claim rejections made under 35 U.S.C. § 112, second paragraph, as indicated in the previous Office action dated September 15, 2009, are withdrawn in view of the claim amendment made by applicant.

Claim rejections made under 35 U.S.C. § 103 (a) indicated in the same Office action are withdrawn and modified without changes to the previous grounds of rejections to address the amended claim limitations and new claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2 6, 7, 9, 13-18, 20, 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Becher (US 6153222) in view of Zerbe et al. (US 6177096 B1).

Becher teaches a dosage form in film of oral application, comprising a mixture of active ingredient, film former, and softeners. See abstract. The reference teaches using crosslinked carboxyvinyl copolymers and/or crosslinked polyvinyl pyrrolidone as film formers. See col. 2, lines 9-12. The reference teaches polyethylene glycol or glycerol as the softener. See Further substances.

The film is supplied with release paper attached thereon, meeting the instant claims 9, 13, and 18.

Becher fails to teach the amount of glycerol as based on the total amount of crosslinked hydrophilic polymers.

Although Becher teaches the active ingredients suitable for the prior art includes dentifrice agents, the reference does not teach the active pharmaceutical ingredients of instant claim 7. See Further substances.

Zerbe teaches a film containing therapeutic agents and/or breath freshening agent for use in the oral cavity. See instant claims 5 and 6. The film comprises water-soluble polymers selected from water-soluble cellulose derivatives and polyacrylates, among others. The reference teaches the film also contains one or more plasticizers. Example 1 teaches a dosage form in film form obtained from a composition comprising 6 g of glycerol and 30 g of hydroxypropylmethyl cellulose (20% of glycerol based on the total amount of the hydrophilic polymer). See instant claims 1 and 3. The suitable pharmaceutical actives for the oral dosage forms include psychoactive drugs, antihistamines, hormones, antibiotics, and chemotherapeutics. See col. 3, lines 16 – 33.

It would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the teachings of Becher by employing glycerol as a softener or plasticizer for the film within the weight amount as taught by Zerbe because both references are directed to dosage forms in film forms that utilize glycerol as a plasticizer and Zerbe discloses the specific weight amount of

glycerol used per the weight amount of film-forming polymers used in such formulations.

Claim 3 now defines the weight range of glycerol to from 30 % to 60 % by weight based on the total amount of crosslinked hydrophilic polymers. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In this case, the utility of a plasticizer as a film softener is taught by Becher and Zerbe, and the latter teaches an operative weight amount of glycerol as plasticizer in a composition comprising a film forming polymer. Discovering by routine experimentations an optimal weight amount of the plasticizer for a different type of polymer such as the crosslinked hydrophilic polymer of Becher would take no more than ordinary skill of the art.

Claims 3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Becher and Zerbe as applied to claims 1, 2, 6, 7, 9, 13-18, 20, 21 as indicated above, and further in view of Mulye (US 6946146 B2).

The references fail to teach the specific type of polymers.

Mulye teaches a polymeric film coating composition for coating a solid dosage form of a medicament, where the coating composition controls the release of the medicament. See abstract. The reference teaches the crosslinked

polymethacrylate and polyacrylate polymers derivatized with hydroxyalkyl and/or ionizable acid or basic functional groups; crosslinked hydroxypropylcellulose are swellable polymer materials. See col. 11, lines 14 – 32. The reference teaches that crosslinked polymers swell in water but will not dissolve, whereas uncrosslinked polymers may dissolve subsequent to swelling. See Id. The reference also teaches crosslinked polyvinyl pyrrolidone or crosslinked polyvinyl alcohol may be used, suggesting functional equivalency of the polymers of Becher and the present claims.

It would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the teachings of the combined references by substituting the crosslinked polymers of Becher with crosslinked hydroxypropylmethylcellulose or crosslinked polyacrylic acid, as motivated by Mulye, because the reference suggests these crosslinked polymers are art-recognized functional equivalents which swell in water without dissolution. The skilled artisan would have had a reasonable expectation of successfully producing a dosage form in film form which swell in water but does not dissolve, by combining the teachings of the references.

Claim 1, 2, 9, 13-19, 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Becher in view of Lydzinski et al. (US 2003/0099692).

Becher is relied upon as discussed above.

Becher fails to teach the amount of glycerol as based on the total amount of crosslinked hydrophilic polymers.

Although Becher teaches the active ingredients suitable for the prior art includes dentifrice agents, the reference does not teach the active pharmaceutical ingredients of instant claim 7. See Further substances.

Lydzinski teaches a dosage form in film form for delivering a variety of agents to a substrate, wherein the active agents may be pharmaceuticals such as dentifrice, antiseptics or agricultural agent such as fertilizers. See [0024]; Instant claims 6-8. The reference teaches plasticizers such as polyols, particularly glycerine, is used in "any desired amount" to increase the apparent flexibility o the film, although the prior art mentions using the plasticizer up to about 15 percent by weight of starch component which forms the bases for the prior art film form. See [0026]. The reference teaches using chemically modified starches well known in the art, including crosslinked starch. See [0013].

It would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the teachings of Becher by applying the prior art film invention to a variety of arts, and formulate a delivery system in film form for a variety of active agents as motivated by Lydzinski.

With respect to the weight range of the plasticizer in present claims 1, 2, and 21, Lydzinski teaches using plasticizers up to about 15 % by weight and further indicates that any desired amount may be employed. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or

workable ranges by routine experimentation." See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Since Lydzinski teaches plasticizers are used in any desired amount, and the purpose of using plasticizer is already known, discovering an optimal weight amount of the plasticizer to obtain desired flexibility would merely require routine experimentations.

Claims 1, 2, 6-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carli et al. (US 5582836) in view of Lydzinski.

Carli discloses a therapeutic composition in film form for transdermal administration of at least one medicament to human, comprising at least one active-ingredient containing layer comprising crosslinked hydrophilic polymers such as crosslinked polyvinyl-pyrrolidone, See col. 2, line 6 - col. 3, line 22; instant claims The reference teaches the transdermal film may be coated with an adhesive film and/or removable protecting sheet. See col. 4, lines 6 – 9; instant claims 9, 10, 18. A person of ordinary skill in the art would have found the term "protecting sheet" to mean that the covering layer is impermeable. See instant claim 20. The medicaments suitable for the invention include analgesics, anesthetics, antihypertensives, antidepressants, hormones, psychoactive drugs, etc. See col. 4, lines 10-33; instant claims 7 and 8. Since the dosage form delivers the active ingredient from the film layer to the substrate, it is obvious that the composition has concentration gradient. See instant claims 11, 19.

Carli fails to teach plasticizers.

Lydzinski teaches a dosage form in film form for delivering a variety of agents to a substrate, wherein the active agents may be pharmaceuticals such

as dentifrice, antiseptics or agricultural agent such as fertilizers. See [0024]; Instant claims 6-8. Also disclosed in topical dosage forms for delivering analgesics and cosmetic agents such as skin bleaching agent, anti-wrinkle agent, and antioxidants, etc. See examples 12-18. The reference teaches plasticizers such as polyols, particularly glycerine, is used in "any desired amount" to increase the apparent flexibility of the film, although the prior art mentions using the plasticizer up to about 15 percent by weight of starch component which forms the bases for the prior art film form. See [0026]. The reference teaches using chemically modified starches well known in the art, including crosslinked starch. See [0013].

It would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the teachings of Carli by incorporating plasticizers such as glycerin as motivated by Lydzinski because 1) both arts are directed to dosage forms in film forms which transdermally deliver pharmaceutical agents to skin and 2) Lydzinski teaches employing plasticizers such as glycerine to increase the apparent flexibility of the film. By combining the teachings of the references, the skilled artisan would have had a reasonable expectation of successfully producing a transdermal film dosage form with improved flexibility.

With respect to the weight range of the plasticizer in present claims 1, 2, and 21, Lydzinski teaches using plasticizers up to about 15 % by weight and further indicates that any desired amount may be employed. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating

such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Since Lydzinski teaches plasticizers are used in any desired amount, and the purpose of using plasticizer is already known, discovering an optimal weight amount of the plasticizer to obtain desired flexibility would merely require routine experimentations.

Response to Arguments

Applicant's arguments filed on January 13, 2010 have been fully considered but they are not persuasive.

Applicant states, "Becher and Zerbe do not contradict the state of the art with respect to plasticizers". As applicant concedes, both references teach and suggest that the utility of a plasticizer to improve pliability and flexibility of film was well known in film composition art.

Applicant asserts a skilled artisan would not have considered glycerol as a required element for the prior art invention. The argument is unpersuasive because the reference clearly teaches the utility of the plasticizer to soften film products.

Applicant also argues that a skilled artisan would have not considered "using 20 % or more of glycerol would not have resulted in phase separations due to crystallization". The argument is not well taken, and applicant provides no support for this assertion.

Applicant asserts Becher and Zerbe are not combinable simply because these two inventions use different type of film forming polymers. The argument is unpersuasive, as both are analogous arts directed to film forming compositions suitable for pharmaceuticals, and both references teach using glycerol to regulate and modify the film-forming properties.

Applicant asserts the combined teachings of the references provide no reasonable expectation of success "especially when both Becher and Zerbe refer to plasticizers as being optional elements". The argument is unpersuasive, as Zerbe discloses a specific formulation comprising glycerol in 20 wt % by weight of a hydrophilic film-forming polymer. The reference would have clearly suggested a skilled artisan that this plasticizer is an essential and preferred component in a dosage form in film form. Both Becher and Zerbe explicitly teach of the utility of a plasticizer and of glycerol in the prior art film compositions, and manipulation of the weight amount of the plasticizer to improve the Becher's film forming composition would have been well within the skill of the art.

Applicant asserts there is evidence of unexpected results, and it appears that applicant is referring to comparative examples 1-4 shown on specification, p. 23, line 30 - p. 25, line 31. Applicant asserts that, according to data, glycerol-containing film forming composition showed "easy handleability and applicability to the human skin and mucous membrane" as compared to compositions comprising polyethylene glycol, sorbitol, trimethyl citrate or no plasticizer. However, such comparison shows no more than a preferred embodiment. The specification merely shows one was "more" difficult or easy to apply on a

substrate, which indicates differences in degree. There is nothing in the record to indicate using glycerol to produce a softer and more flexible film forming composition was surprising at the time of the present invention. On the contrary, the prior arts clearly suggest such utility was notoriously well known to one of ordinary skill in pharmaceutical art.

Applicant argues the Cali /Lydzinski refection is "essentially a duplicate rejection of Becher and Zerbe with the same attendant problems". Examiner respectfully disagrees. The Becher/Zerbe and Cali/Lydzinski rejections are not duplicate or based on duplicate grounds of rejections. For example, claim 8 was addressed only in the Cali/Lydzinski rejection, as only Lydzinski teaches of applying a film forming composition for delivery of a fertilizer. If the rejections appear duplicate having similar problems (i.e., utilizing a plasticizer in a film-forming composition to improve the film properties), it is because the examiner adhered to the patent law to cite only the prior art arts that are pertinent to applicant's endeavor and to the particular problem that applicant was trying to solve. See In re Oetiker, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). Applicant's remarks here are viewed as an admission that the cited arts are analogous and therefore properly combinable.

Applicant states Cali is "an even weaker reference". The argument is not well taken, since the reference is on the point to teach that the film-forming polymer of the rejected claims had been well known in the art for the same utility of the present invention.

Applicant asserts Lydzinski's reference to "'any desired amount' would have been in amounts greater than that thought possible by those of skill in the art". The argument is not well taken, as it is well settled in patent law that manipulating the weight amount of a component to find an optimal weight range only takes ordinary skill in chemical art. See In re Aller. In this case, the reference teaches a specific example of using a plasticizer in an amount of 15 wt % based on a film forming polymer in composition, and even suggests to manipulate the plasticizer amount. The function of a plasticizer is well known in the art. There is nothing unobvious about discovering an optimal weight range of a well known adjuvant which is used for the very same purpose used in the prior arts.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINA C. YU whose telephone number is (571)272-8605. The examiner can normally be reached on Monday through Thursday, from 8:00AM until 6:00 PM..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GINA C. YU/
Primary Examiner, Art Unit 1611